IAP10 Rec'd PCT/PTO 22 DEC 2005

FILING BY "EXPRESS MAIL" UNDER 37 CFR 1.10

EV 704620613 US

Express Mail Label Number

22 December 2005 Date of Deposit

Form PTO-1390-MOD (REV 10-96) U. S. Department of Commerce Patent and Trademark Office ATTORNEY'S DOCKET NUMBER PN/4-33159A U.S. APPLICATION NO. (If known, see 37 CFR 1.5) TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) 10/561949 CONCERNING A FILING UNDER 35 U.S.C. 371 INTERNATIONAL APPLICATION NO. PRIORITY DATE CLAIMED INTERNATIONAL FILING DATE PCT/EP 2004/007247 2 July 2004 (02.07.04) 3 July 2003 (03.07.03) TITLE OF INVENTION MACROCYCLIC COMPOUNDS HAVING ASPARTIC PROTEASE INHIBITING ACTIVITY AND PHARMACEUTICAL **USES THEREOF** APPLICANT(S) FOR DO/EO/US BETSCHART ET AL. Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information: This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay 3. examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1). A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority 5. \boxtimes A copy of the International Application as filed (35 U.S.C. 371(c)(2)) is transmitted herewith (required only if not transmitted by the International Bureau). has been transmitted by the International Bureau. (See Form PCT/IB/308) is not required, as the application was filed in the United States Receiving Office (RO/US). A translation of the International Application into English (35 U.S.C. 371(c)(2)). Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C.371(c)(3)). are transmitted herewith (required only if not transmitted by the International Bureau). have been transmitted by the International Bureau. have not been made; however, the time limit for making such amendments has NOT expired. have not been made and will not be made. A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)). An executed Declaration and Power of Attorney (original or copy) (35 U.S.C. 371(c)(4)). A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). Items 11. to 16. below concern document(s) or information included. 11. An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 12. An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. A FIRST preliminary amendment. A SECOND or SUBSEQUENT preliminary amendment. 14. An Application Data Sheet under 37 CFR 1.76. 15. A substitute specification. 16. A change of power of attorney and/or address letter. 17. A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821-1.825. 18. A second copy of the published International Application under 35 U.S.C. 154(d)(4). 19. A second copy of the English language translation of the International application under 35 U.S.C. 154(d)(4). 20.
Other items or information:

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| PCT/EP 2004/007247 PN/4-331 The following fees are submitted: | | | | | | | | | | | CALCULATIONS PTO USE | | | |
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| 21. | | | | | | | | | |) | | | | |
| 22. Examination Fee If International preliminary examination report was prepared by USPTO and all claims satisfy provisions of PCT Article 33(1)-(4) | | | | | | | | | | | | | | |
| | | | | | | | | | |) | | | | |
| 23. Search fee ☐ If Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority \$ ☐ If International Search Report was prepared and provided to the Office \$400 ☐ All other situations | | | | | | | | | |) | | | | |
| TOTAL OF 21, 22 AND 23 = | | | | | | | | | | | \$ | 900 | | |
| Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper of thereof. | | | | | | | | | | | comput | er | | |
| Total Sheets | | | | | | | | | | | | | | - |
| 35 - 100 = | | /50 = | | | 0 | 112017 | X | \$ | 250 | | \$ | | | |
| Surcharge of \$130 for furnishing the oath of declaration later than months from the earliest claimed priority date (37 CFR 1.492(e)). | | | | | | | | | | | \$ | | | |
| CLAIMS | | NUMBE | RFILED |) | NUMBER EXT | RA | | RA | ΤĘ | | | | | |
| Total claims | | 11 | 0 = | 0 | | Х | \$ | 50 | | \$ | | | | |
| Independent claims 1 -3 = 0 X \$ 200 MULTIPLE DEPENDENT CLAIM(S) (if applicable) + \$ 360 | | | | | | | | | | \$ | | | | |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable) + \$ 360 TOTAL OF ABOVE CALCULATIONS = | | | | | | | | | | | <u>\$</u> \$ | 900 | | |
| Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be | | | | | | | | | | | 300 | | | |
| filed (Note 37 CFR 1.9, 1.27, 1.28). SUBTOTAL = | | | | | | | | | | <u>\$ </u> | 900 | | | |
| Processing fee of \$130 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(f)). | | | | | | | | | | \$ \$ | - | | | |
| TOTAL NATIONAL FEE = | | | | | | | | | | \$ \$ | 900 | | | |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40 per property + | | | | | | | | | d | \$ | | | | |
| TOTAL FEES ENCLOSED = | | | | | | | | | | \$ | 900 | | | |
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| The Commissioner is hereby authorized to charge any additional fees which may be required, on Deposit Account No. 19-0134 in the name of Novartis. | | | | | | | | | | | | ny ove | erpayment | to |
| NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status. | | | | | | | | | | | | | a) | |
| Send all correspondence to the address associated with Customer No. 001095, which is currently: | | | | | | | | | | | | | | |
| One Hea | te Intelle alth Plaza | ctual Proper a, Building 1 J 07936-108 | 04 | | | Attorr Reg. | J. Wai ney for No. 43 778-79 | Applic ,228 | ants | | | -100 | | |